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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/107,979	06/30/98	GODOWSKI	P F1084R1-2

GENENTECH INC
ATTN: DEIRDRE L CONLEY
1 DNA WAY
SOUTH SAN FRANCISCO CA 94080

HM22/1130

EXAMINER

LEE, L

ART UNIT

1645

PAPER NUMBER

DATE MAILED:

11/30/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.
09/107,979

Applicant(s)
Godowaki et al

Examiner
LI Lee

Group Art Unit
1645



☒ Responsive to communication(s) filed on Sep 13, 1999

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 35 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) 1-38 is/are pending in the applicat

Of the above, claim(s) 1-28 and 33-38 is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 29-32 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☒ Claims 1-38 are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 5

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

— SEE OFFICE ACTION ON THE FOLLOWING PAGES —

Art Unit: 1645

DETAILED ACTION

Election/Restriction

1. Applicant's election of Group VI, claims 29-32 in Paper No. 7 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Drawings

2. This application has been filed with informal drawings which are acceptable for examination purposes only. The drawings are objected to by the draftsman under 37 C.F.R. 1.84 or 1.152. See PTO-948 for details. Correction of the noted defects can be deferred until the application is allowed by the examiner.

Information Disclosure Statement

3. Items listed on form PTO-1449 filed on Jan 11, 1999 have been considered by the examiner.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Art Unit: 1645

5. Claims 29-32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 29-32 are incomplete for depending from non-elected claim 1.

Applicant is reminded that claim 1 contains a indefinite and confusing term "an amino acid sequence encoding an EGF-like domain". The art teaches that a DNA sequence encodes a protein, but not an amino acid sequence encoding a protein. *An amino acid sequence is a protein, it does not encode a protein. MPA 11/29/99*

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 29 and 31-32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polypeptide of SEQ ID NO:4, does not reasonably provide enablement for any variant of polypeptide of SEQ ID NO:4. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 29 and 31-32 are drawn an immunoadhesin comprising a polypeptide comprising an amino acid sequence of an EGF-like domain which has the binding characteristics of NRG3, wherein the polypeptide fused to an immunoglobulin constant domain sequence of an IgG-1, IgG-2, or IgG-3.

Art Unit: 1645

This encompasses any polypeptide variant of the polypeptide SEQ ID NO:4 which has the binding characteristics of NRG3 fused to an immunoglobulin constant domain as an immunoadhesin. However, the specification only teaches an immunoadhesin which is made of the polypeptide EGF-like domain of SEQ ID NO:4 (page 43, lines 16-17) and an immunoglobulin constant domain. The specification fails to teach the specific binding characteristics of NRG3 for such EGF-like domain and without such information, one skilled in the art can not know when the limitations for the EGF-like domain have been met. The art teaches that the neuregulins gene encodes a large number of alternatively spliced transcripts, most of which encode integral membrane proteins containing EGF-like domain (Zhang, et al. PNAS 94:9562, 1997). Without clearly characterization of the NRG3 binding activity, one skilled in the art could not predict which EGF-like domain out of the large number of known EGF-like domains would have a the EGF-like domain in a manner similar to the polypeptide of SEQ ID NO:4. Furthermore, the specification is not enabled for protein variants of SEQ ID NO:4 because the specification fails to teach what are the critical protein portions that are needed for the binding characteristics of NRG3 activity. Protein chemistry is probably one of the most unpredictable areas of biotechnology and the art teaches that the significance of any particular amino acid and sequences for different aspects of biological activity can not be predicted *a priori* and must be determined empirically on a case by case basis (Rudinger et al., in "Peptide Hormones", edited by Parsons, J.A., University Park Press, June 1976, page 6). The art specifically teaches that even a single amino acid change in a protein leads to unpredictable change in the biological activity of the

Art Unit: 1645

protein. For example, replacement of a single lysine residue at position 118 of the acidic fibroblast growth factor by glutamic acid led to a substantial loss of heparin binding, receptor binding, and biological activity of the protein (Burgess et al., The Journal of Cell Biology, 111:2129-2138, 1990). In view of the lack of specific characteristics for the NRG3 binding activity, the lack of any guidance of any protein variant that functions equivalently to the protein of SEQ ID NO:4, the lack of an enabling description of how to obtain and make the amino acid variants of SEQ ID NO:4, the unpredictability associated with making the variants of SEQ ID NO:4 encompassed in the scope of the claims as set forth above, the skilled artisan would be forced into undue experimentation to practice (i.e. make) the invention as is broadly claimed.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

8. Claims 29 and 31-32 are rejected under 35 U.S.C. 102(b) as being anticipated by Wei-Hsien Ho et al (WO 96/15244, May 23, 1996).

Art Unit: 1645

In order to advance prosecution, claims 29 and 31-32 read on an immunoadhesin including the limitation of claim 1 and the claim 1 reads on a polypeptide comprising an amino acid sequence of an EGF (epidermal growth factor)-like domain (not an amino acid sequence encoding an EGF-like domain because an amino acid sequence cannot encode a protein domain), wherein the amino acid sequence has the binding characteristics of NRG3 (e.g., to bind neuregulin receptor and stimulate cellular responses, page 20, lines 25-27). Therefore, claims 29 and 31-32 are drawn and encompass to an immunoadhesin comprising a polypeptide comprising an amino acid sequence of an EGF-like domain which bind neuregulin receptor and stimulate cellular responses, wherein the polypeptide fused to an immunoglobulin constant domain sequence of an IgG-1, IgG-2, or IgG-3.

Wei-Hsien Ho et al teach an immunoadhesin comprising a polypeptide (SMDF) comprising an amino acid sequence of an EGF-like domain (β -type EGF-like domain) which bind neuregulin receptor and stimulate cellular responses/mitogenic activity, wherein the polypeptide fused to an immunoglobulin constant domain sequence of an IgG-1, IgG-2, or IgG-3 (Abstract, page 10, lines 22-27).

9. Claims 29 and 31-32 are rejected under 35 U.S.C. 102(e) as being anticipated by Capon et al (US 5714147, Feb 3, 1998).

Capon et al teach an immunoadhesin comprising a polypeptide (ligand binding partner, LHR) comprising an amino acid sequence of an EGF (epidermal growth factor)-like domain which bind neuregulin receptor and stimulate cellular responses/mitogenic activity column 7, lines

Art Unit: 1645

19-57), wherein the polypeptide fused to an immunoglobulin constant domain sequence of an IgG-1, IgG-2, or IgG-3 (Abstract and columns 13, lines 58-67).

Allowable Subject Matter

10. Claim 30 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Status of Claims


11. No claims are allowed. All claims stand rejected.

Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1645 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Li Lee, M.D., Ph.D. whose telephone number is (703) 308-8891. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached at (703) 308-3995.

Li Lee, M.D., Ph.D.
November 26, 1999


MARIANNE P. ALLEN
PRIMARY EXAMINER
GROUP 1600
AU 1645